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(71) Applicants (for all designated States except US): GLAXO-
OSMITHKLINE BIOLOGICALS S.A. [BE/BE]; Rue de
l'Institut 89, B-1330 Rixensart Brussels (BE). GLAXO
GROUP LIMITED [GB/GB]; Glaxo Wellcome House,
Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): CABEZON

SILIVA, Teresa, Elisa, Virginia [BE/BE]; Glaxo-
SmithKline Biologicals s.a., Rue de l'Institut 89, B-1330
Rixensart Brussels (BE). ELLIS, Jonathan, H. [GB/GB];
GlaxoSmithKline, Gunnels Wood Road, Stevenage,
Hertfordshire SG1 2NY (GB). GERARD, Catherine,
Marie, Ghislaine [BE/BE]; GlaxoSmithKline Biologicals
s.a., Rue de l'Institut 89, B-1330 Rixensart Brussels
(BE). HAMBLIN, Paul, A. [GB/GB]; GlaxoSmithKline,
Gunnels Wood Road, Stevenage, Hertfordshire SG1
2NY (GB). PALMANTIER, Remi, M. [FR/BE]; Glaxo-
SmithKline Biologicals s.a., Rue de l'Institut 89, B-1330
Rixensart Brussels (BE). VINALS Y DE BASSOLS,
Carlota [BE/BE]; GlaxoSmithKline Biologicals s.a., Rue
de l'Institut 89, B-1330 Rixensart Brussels (BE).

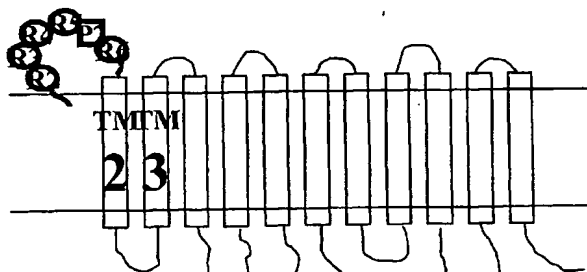
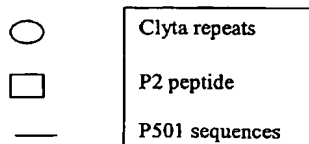
(74) Agent: DALTON, Marcus, Jonathan, William; Glaxo-
SmithKline, CN925.1, 980 Great West Road, Brentford,
Middlesex TW8 9GS (GB).

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,

[Continued on next page]

(54) Title: IMMUNOGENIC COMPOSITIONS

Structure of CPC-p501 His fusion protein expressed in *S. cerevisiae*



(57) Abstract: The present invention relates fusion partners which act as immunological fusion partners, as expression enhancers, and preferably to fusion partners having both functions. In particular the fusion partners contain a so-called choline binding domain, for example fusions comprising LytA from *Streptococcus pneumoniae*, or the pneumococcal phage CP1 lysozyme (CPL1) wherein the choline binding domain is modified to include a heterologous T-helper epitope, and are fused to antigens, particularly poorly immunogenic antigens such as self-antigens, eg tumour specific or tissue specific antigens. The invention also relates to fusion proteins containing them, to their manufacture, to their use in immunogenic compositions and vaccines and to their use in medicines.



MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/315 A61K39/385 C12N5/10 C12N15/62 C12N15/63
A61K38/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, MEDLINE, SEQUENCE SEARCH, BIOSIS, EPO-Internal, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>SANCHEZ-PUELLES J M ET AL: "IMMOBILIZATION AND SINGLE-STEP PURIFICATION OF FUSION PROTEINS USING DEAE-CELLULOSE" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 203, no. 1-2, 1992, pages 153-160, XP001155694 ISSN: 0014-2956 the whole document</p> <p style="text-align: center;">--- -/--</p>	1-27

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Mossier, B

INTERNATIONAL SEARCH REPORT

Internat Application No
PCT/EP 03/06096

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CAUBIN J ET AL: "Choline-binding domain as a novel affinity tag for purification of fusion proteins produced in <i>Pichia pastoris</i> " BIOTECHNOLOGY AND BIOENGINEERING, vol. 74, no. 2, 20 July 2001 (2001-07-20), pages 164-171, XP001155696 ISSN: 0006-3592 the whole document ---	1-27
A	KJERRULF M ET AL: "TANDEM REPEATS OF T HELPER EPITOPES ENHANCE IMMUNOGENICITY OF FUSION PROTEINS BY PROMOTING PROCESSING AND PRESENTATION" MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 34, no. 8/9, June 1997 (1997-06), pages 599-608, XP000857056 ISSN: 0161-5890 the whole document ---	1-27
A	ASTORI M ET AL: "RECOMBINATION FUSION PEPTIDES CONTAINING SINGLE OR MULTIPLE REPEATS OF A UBIQUITOUS T-HELPER EPITOPE ARE HIGHLY IMMUNOGENIC" MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 33, no. 13, 1996, pages 1017-1024, XP001028964 ISSN: 0161-5890 the whole document ---	1-27
A	OLSZEWSKA WIESLAWA ET AL: "Protection against measles virus-induced encephalitis by anti-mimotope antibodies: The role of antibody affinity" VIROLOGY, vol. 272, no. 1, 30 June 2000 (2000-06-30), pages 98-105, XP002259121 ISSN: 0042-6822 the whole document ---	1-27
A	WO 99 67293 A (UNITED BIOMEDICAL INC ; WANG CHANG YI (US); WALFIELD ALAN M (US)) 29 December 1999 (1999-12-29) abstract ---	1-27
A	US 6 090 388 A (WANG CHANG YI) 18 July 2000 (2000-07-18) abstract -----	1-27

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/06096

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 26 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

ation on patent family members

Interna pplication No

PCT/EP 03/06096

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9967293	A	29-12-1999	AU 757919 B2	13-03-2003
			AU 4580299 A	10-01-2000
			BR 9911389 A	20-03-2001
			CA 2329754 A1	29-12-1999
			CN 1305498 T	25-07-2001
			EP 1090039 A1	11-04-2001
			JP 2002518038 T	25-06-2002
			WO 9967293 A1	29-12-1999
			ZA 200006384 A	29-05-2001
<hr/>				
US 6090388	A	18-07-2000	AU 4704899 A	10-01-2000
			BR 9912175 A	10-04-2001
			CA 2330235 A1	29-12-1999
			CN 1303394 T	11-07-2001
			EP 1098910 A1	16-05-2001
			JP 2002518523 T	25-06-2002
			WO 9967294 A1	29-12-1999
			ZA 200006385 A	11-10-2001
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